Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections (Review)

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[Intervention Review]

Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

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ABSTRACT

Background

Cesarean delivery is one of the most common surgical procedures performed by obstetricians. Infectious morbidity after cesarean delivery can have a tremendous impact on the postpartum woman's return to normal function and her ability to care for her baby. Despite the widespread use of prophylactic antibiotics, postoperative infectious morbidity still complicates cesarean deliveries.

Objectives

To determine if cleansing the vagina with an antiseptic solution before a cesarean delivery decreases the risk of maternal infectious morbidities, including endometritis and wound complications.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (21 July 2014).

Selection criteria

We included randomized and quasi-randomized trials assessing the impact of vaginal cleansing immediately before cesarean delivery with any type of antiseptic solution versus a placebo solution/standard of care on post-cesarean infectious morbidity.

Data collection and analysis

We independently assessed eligibility and quality of the studies.

Main results

Five trials randomizing 1946 women (1766 analyzed) evaluated the effects of vaginal cleansing (all with povidone-iodine) on post-cesarean infectious morbidity. The risk of bias was generally low, with the quality of most of the studies being high. Vaginal preparation immediately before cesarean delivery significantly reduced the incidence of post-cesarean endometritis from 7.2% in control groups to 3.6% in vaginal cleansing groups (average risk ratio (RR) 0.39, 95% confidence interval (CI) 0.16 to 0.97, five trials, 1766 women). The risk reduction was particularly strong for women with ruptured membranes (1.4% in the vaginal cleansing group versus 15.4% in the

control group; RR 0.13, 95% CI 0.02 to 0.66, two trials, 148 women). No other outcomes realized statistically significant differences between the vaginal cleansing and control groups. No adverse effects were reported with the povidone-iodine vaginal cleansing.

The quality of the evidence using GRADE was low for post-cesarean endometritis, moderate for postoperative fever, and low for wound infection.

Authors' conclusions

Vaginal preparation with povidone-iodine solution immediately before cesarean delivery reduces the risk of postoperative endometritis. This benefit is particularly realized for women undergoing cesarean delivery with ruptured membranes. As a simple, generally inexpensive intervention, providers should consider implementing preoperative vaginal cleansing with povidone-iodine before performing cesarean deliveries.

PLAIN LANGUAGE SUMMARY

Vaginal cleansing before cesarean delivery to reduce post-cesarean infections

Cesarean deliveries are very common today, with almost one in three babies born by cesarean in some countries. Antibiotics are routinely given before or during the surgery to reduce the risk of infections, but some women still suffer from these complications. Between one in four and one in 10 women develop an infection of the uterus (endometritis) or a problem with their skin incision, respectively. These complications slow recovery from the surgery and may affect the mother's ability to take care of her baby. Other interventions are needed to further reduce the risk of infections of the uterus and wound problems after cesarean delivery.

This review found that cleansing the vagina with an antiseptic solution immediately before the cesarean delivery reduced the risk of post-cesarean infection of the uterus (womb) (low quality of evidence). The benefit was greater if the woman's water had already broken (the membranes had ruptured). This review did not find that vaginal cleansing reduced the number of women experiencing fever or wound complications after cesarean delivery. The antiseptic was povidone-iodine, and no adverse events such as allergy or irritation were noted in any of the five randomized trials, reporting on 1766 women, from vaginal preparation solution.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Vaginal preparation versus control for preventing postoperative infections

Population: Pregnant women who received a cesarean delivery
Settings: A hospital in Iran and hospitals in USA
Intervention: Vaginal preparation with povidone-iodine solution versus control (saline vaginal wash; no vaginal cleansing)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Vaginal preparation versus control				
Post-cesarean endometritis	Study population		RR 0.39 (0.16 to 0.97)	1766 (5 studies)	⊕⊕◯◯ **low**[1,2]	
	72 per 1000	28 per 1000 (12 to 70)				
	Moderate					
	75 per 1000	29 per 1000 (12 to 73)				
Postoperative fever	Study population		RR 0.92 (0.71 to 1.18)	1606 (4 studies)	⊕⊕⊕◯ **moderate**[2,3]	
	134 per 1000	123 per 1000 (95 to 158)				
	Moderate					
	117 per 1000	108 per 1000 (83 to 138)				
Wound infection	Study population		RR 0.99 (0.57 to 1.7)	1336 (4 studies)	⊕⊕◯◯ **low**[2,4,5]	

	37 per 1000	**37 per 1000** (21 to 63)		
	Moderate			
	41 per 1000	**41 per 1000** (23 to 70)		

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Statistical heterogeneity ($I^2 > 60\%$).
[2] Optimal information size not met.
[3] Confidence interval crossing the line of no effect.
[4] Half of the studies contributing data had design limitations.
[5] Wide confidence interval crossing the line of no effect.

BACKGROUND

Cesarean sections currently account for approximately one-third of the babies born in the United States. Cesarean section deliveries are often complicated by infections occurring after the surgery.

Description of the condition

Endometritis, an infection of the uterus in the postpartum period, can complicate the postoperative course of a cesarean delivery 6% to 27% of the time (Guzman 2002; Hofmeyr 2002). This complication, up to 10 times more frequent after a cesarean delivery than after vaginal delivery, can lead to serious complications of bacterial infection in the blood (10% to 20%), peritonitis (general infection in the abdominal cavity), intra-abdominal abscess (cavity filled with infected material), and sepsis (French 2004; Yokoe 2001). Additionally, cesarean deliveries are frequently complicated by maternal fever and wound complications including seroma (fluid collection under the skin), hematoma (blood clots under the skin), infection, and separation. These morbidities can lead to significant delay in a return to normal function.

Fevers and infections after cesarean deliveries are associated with the length of ruptured membranes, length of labor, and number of vaginal examinations (Disgupta 1988; Yonekura 1985). Post-cesarean endometritis and infectious morbidity are the result often of the presence of bacteria in the vagina and cervix that move higher in the genital tract to infect the uterus (Martens 1991). These bacteria have been shown to be responsible for failure of antibiotic prophylaxis during cesarean deliveries (Watts 1991). Additionally, some antibiotics do not consistently eradicate some bacteria (such as *enterococcus*) and the vagina has been shown to become colonized with antibiotic-resistant bacteria after preoperative surgical antibiotic prophylaxis (Gibbs 1982; Graham 1993; Stiver 1984). Currently, it is standard care to give antibiotics to women receiving a cesarean delivery, but the rate of post-cesarean infections remains a problem.

Description of the intervention

Previous studies have evaluated whether vaginal cleansing before a cesarean delivery with various solutions can reduce the incidence of febrile morbidity (endometritis and wound infections). Povidone iodine, chlorhexidine, and vaginal metronidazole have been reported with varying results. Older data comparing iodine with chlorhexidine before hysterectomy showed lower morbidity in the iodine group, with improved activity against anaerobic pathogens (Duignan 1975; Haeri 1984). Currently, it is not standard care in the United States to prepare the vagina with an antiseptic solution before cesarean delivery. Vaginal cleansing solutions such as chlorhexidine and povidone iodine have very few side effects in general, with low rates of noted allergies or irritation symptoms.

How the intervention might work

By cleansing the vagina of bacteria before the cesarean delivery occurs, there may be less of a bacterial load in the vagina that might cause infectious morbidity postoperatively. As ascending infection is thought to be a major etiology of postoperative endometritis, this could logically reduce that risk.

Why it is important to do this review

Cesarean delivery is increasing, particularly in the developed world. Postoperative infectious morbidity after cesarean delivery impacts the woman's return to normal function and potentially her bonding with the newborn. It can also cause major medical problems and sequelae. Finding an easy, inexpensive method to reduce this risk could have major public health impact in both developed and developing countries.

OBJECTIVES

Our objective was to determine if cleansing the vagina with an antiseptic solution before a cesarean delivery decreases the risk of maternal morbidities, including endometritis and wound complications. We also assessed the side effects of vaginal cleansing solutions to determine adverse events associated with the intervention.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomized and quasi-randomized studies.

Types of participants

Pregnant women who received a cesarean delivery.

Types of interventions

Any method of vaginal cleansing (including douches, wipes, sponges, etc.) with any type of antiseptic solution (povidone iodine, chlorhexidine, etc.) versus a placebo solution/standard care (no vaginal preparation).

We included only studies where vaginal preparation was performed no more than one hour before surgery. This review addressed the use of preoperative vaginal cleansing after the decision to perform a cesarean had been made. This review did not address the use of vaginal preparation during labor. Thus, we excluded trials utilizing

vaginal cleansing solutions during labor. We also excluded studies where prophylactic surgical antibiotics were explicitly not used. Surgical prophylaxis with intravenous antibiotics before or during cesarean deliveries has been clearly demonstrated as beneficial in reducing postoperative infectious morbidities. Thus, it is the standard of care. Inclusion of trials not utilizing general surgical antibiotic prophylaxis would not represent the current standard of care and the results would not be translatable into current practice.

Types of outcome measures

Primary outcomes

Postpartum endometritis: defined as a clinical diagnosis, usually involving fever, uterine fundal tenderness, or purulent lochia requiring antibiotic therapy.

Secondary outcomes

- Postoperative wound infection: defined as erythema, tenderness, purulent drainage from the incision site, with or without fever, requiring antibiotic therapy.
- Postoperative fever: defined as greater than 38 degrees C or 100.4 degrees F.
- Postoperative wound seroma or hematoma: defined as collection of serous fluid or blood/clot in the subcutaneous area of the incision.
- Composite wound complications: defined as the presence of any one of the following: wound infection, seroma, hematoma, separation.
- Composite wound complications or endometritis.
- Side effects of vaginal preparation (allergy, irritation). As these solutions are applied gently and not absorbed, there should be no adverse fetal/neonatal effects. We did not anticipate or find mention of adverse neonatal effects from the vaginal cleansing.

Search methods for identification of studies

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Electronic searches

We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (21 July 2014).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of Embase;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and Embase, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We did not apply any language restrictions.

Data collection and analysis

For the methods used when assessing the trials identified in the previous version of this review, *see* Haas 2013.

For this update, no new studies were identified. We will use the methods outlined in Appendix 2 for new trials identified at the next update.

We used the following updated methods to assess the risk of bias and assess the quality of already included studies using the GRADE approach. The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Selection of studies

All three review authors independently assessed for inclusion all the potential studies identified as a result of the search strategy. We resolved any disagreement through discussion.

Data extraction and management

We designed a form to extract data. For eligible studies, all three review authors extracted the data using the agreed form. We resolved discrepancies through discussion. We entered data into Review Manager software (RevMan 2011).

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Three review authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved any disagreement by discussion.

(1) Random sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.
We assessed the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.
We assessed the methods as:

- low risk of bias (e.g. telephone or central randomization; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.
We assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.
We assessed methods used to blind outcome assessment as:

- low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total number of randomized participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we planned to re-include missing data in the analyses.
We assessed methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers (> 20%) or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomization);
- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found.
We assessed the methods as:

- low risk of bias (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We described for each included study any important concerns we had about other possible sources of bias.
We assessed whether each study was free of other problems that could put it at risk of bias:

- low risk of other bias;
- high risk of other bias;
- unclear whether there is risk of other bias.

(7) Overall risk of bias

We made explicit judgements about whether studies were at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it likely to impact on the findings. In future updates, if

more studies are included, we will explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

For this update, the quality of the evidence was assessed using the GRADE approach (Schunemann 2009) in order to assess the quality of the body of evidence relating to the following outcomes for the main comparisons.

1. Postpartum endometritis.
2. Postoperative wound infection.
3. Postoperative fever.

GRADEprofiler (Grade 2008) was used to import data from Review Manager 5.3 (RevMan 2014) in order to create a 'Summary of findings' table. A summary of the intervention effect and a measure of quality for each of the above outcomes was produced using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

Continuous data

For continuous data, we planned to use the mean difference if outcomes were measured in the same way between trials. We planned to use the standardized mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomized trials

There were no cluster-randomized trials. If in future updates some are identified, we will include cluster-randomized trials in the analyses along with individually-randomized trials. We will adjust their sample sizes using the methods described in the *Handbook* (Higgins 2011) using an estimate of the intracluster correlation coefficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomized trials and individually-randomized trials, we plan to synthesize the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomization unit is considered to be unlikely.

We will also acknowledge heterogeneity in the randomization unit and perform a sensitivity analysis to investigate the effects of the randomization unit.

Cross-over trials

Cross-over trials are not possible for this intervention and are not included.

Other unit of analysis issues

We included quasi-randomized trials but noted their increased risk of bias in this design.

Dealing with missing data

For included studies, we noted levels of attrition. We did not encounter large levels of attrition. In future updates, if we do encounter large levels of attrition, we will explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we carried out analyses, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomized to each group in the analyses, and all participants were analyzed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial was the number randomized minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the Tau^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if the I^2 was greater than 30% and either a Tau^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

There are only five studies included. If there are 10 or more studies in the meta-analysis at a future update, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually. If asymmetry is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2011). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. The random-effects summary was treated as the average range of possible treatment effects and we discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we did not combine trials.

Where we used random-effects analyses, the results are presented as the average treatment effect with 95% confidence intervals, and the estimates of Tau^2 and I^2.

Subgroup analysis and investigation of heterogeneity

In future updates, if we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, use random-effects analysis to produce it.

For this update, we carried out the following subgroup analyses.

1. Women in labor versus women not in labor.
2. Women with ruptured membranes versus women with intact membranes.
3. Women with chorioamnionitis preoperatively versus women without chorioamnionitis.
4. Women undergoing emergency cesarean versus those undergoing unscheduled cesarean versus those undergoing scheduled cesarean.
5. Women with internal fetal or uterine monitors in place versus those with only external monitors in place before the cesarean.

All reported outcomes in the primary analysis were used in the subgroup analyses.

We assessed subgroup differences by interaction tests available within RevMan (RevMan 2011). We reported the results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2 value.

Sensitivity analysis

We did not perform any sensitivity analyses due to a lack of studies included within analyses. In future updates, we plan to carry out sensitivity analyses to explore the effect of trial quality assessed by concealment of allocation, high attrition rates (> 20%), or both, with poor quality studies being excluded from the analyses, in order to assess whether this makes any difference to the overall result.

RESULTS

Description of studies

Results of the search

The original search yielded six reports of four studies. The search of the Pregnancy and Childbirth Group's Trials Register conducted in August 2012 resulted in three further trial reports. One was the published report of Haas 2010 and the other two were reports of one trial Asghania 2011. We obtained full data from the authors. The 2014 search did not identify any new reports for our consideration.

Included studies

All five studies qualified for inclusion in this review. All five studies compared preoperative vaginal povidone-iodine solution preparation with a control group. In one trial (Guzman 2002), the control group was a saline vaginal wash. The other four trials compared the vaginal cleansing with no vaginal cleansing (Asghania 2011; Haas 2010; Reid 2001; Starr 2005).

Excluded studies

No studies were excluded.

Risk of bias in included studies

See 'Risk of bias' tables for the five included studies in Characteristics of included studies and Figure 1; and Figure 2, for summaries of 'Risk of bias' assessments. Overall, the quality of these five studies was generally high as defined by Higgins 2008. Most of the information for the review is derived from studies at low risk of bias. All the studies reported on the outcome of endometritis, while four reported on postoperative fever and wound infection. Two studies reported any wound complication and only one study reported a composite of endometritis or any wound complication. One trial excluded women with chorioamnionitis (Starr 2005). Two trials excluded women undergoing emergency cesarean deliveries (Guzman 2002; Reid 2001).

Figure 1. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

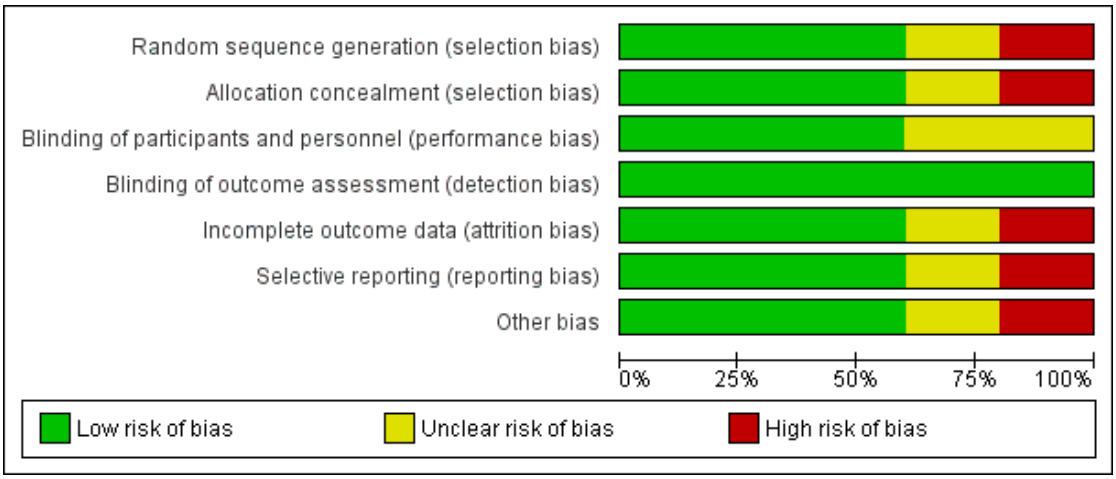
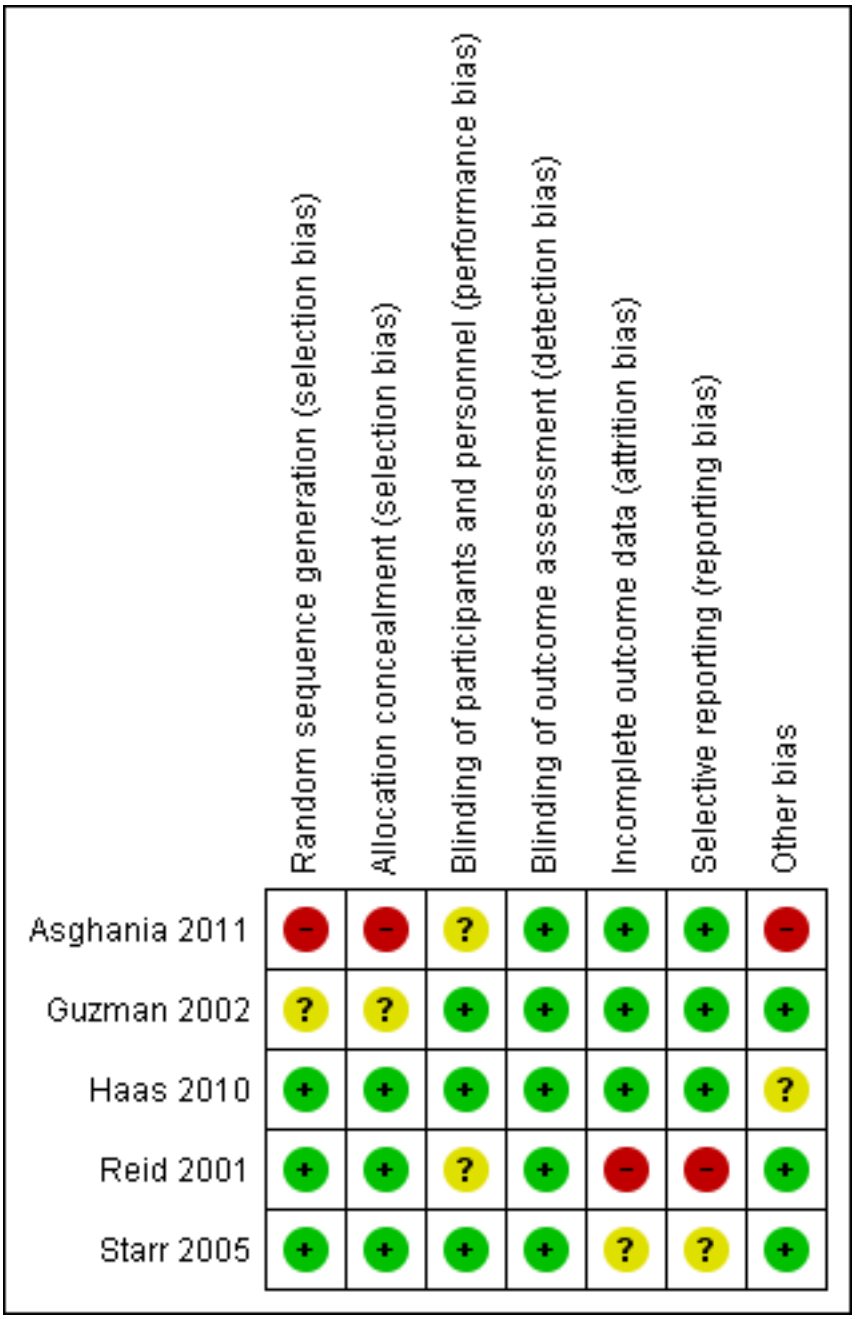


Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Allocation

Only the Guzman 2002 study was unclear about the randomization sequence generation and allocation concealment.The trial, however, appeared free of any other biases. One study (Asghania 2011) was a quasi-randomized trial with alternate allocation.

Blinding

All five trials blinded outcomes assessors and most had some mechanism for blinding of providers or were unclear about whether participants were blinded.

Incomplete outcome data

Only the Reid 2001 study was felt to potentially have incomplete outcome bias. This stems from the post-hoc exclusion of women with chorioamnionitis.

Selective reporting

One trial (Reid 2001) had a large number of participants excluded after randomization who had chorioamnionitis (a known risk factor for postoperative infectious morbidity) because their inclusion "distorted the absolute rates of fever and infectious morbidity." That trial states that when the 68 participants with antepartum infection were included, the estimates of effect of vaginal preparation were not meaningfully different. Thus they planned to exclude those participants from reports of outcomes. As this represented 13.5% of the originally randomized sample, however, there is a risk that this introduced selective reporting bias into the trial (Reid 2001). One other trial had a potential selective reporting bias (Starr 2005). Of 400 participants randomized, 92 (23%) were excluded after randomization: 33 due to lost envelopes, six for violations of inclusion criteria, and 53 because their hospital charts could not be located. Of all the women excluded, 54 were in the vaginal cleansing group and 38 were in the control group. Only outcomes for women for whom all data were available were reported. The large number of women excluded also makes this trial subject to an unclear risk of bias, however as there is no outcome data for the excluded participants, the potential impact is unclear (Starr 2005).

Other potential sources of bias

One trial (Haas 2010) was stopped early at a planned safety analysis due to difficulty recruiting participants. The Asghania 2011 trial excluded women with potential infection before the surgery, including chorioamnionitis, but this was done before enrollment.

Effects of interventions

See: **Summary of findings for the main comparison** Vaginal preparation versus control for preventing postoperative infections

We included five trials involving 1946 randomized women (1766 analyzed). One trial (Guzman 2002) compared vaginal povidone-iodine with a saline vaginal preparation. The remaining four trials compared vaginal povidone-iodine with no vaginal cleansing (Asghania 2011; Haas 2010; Reid 2001; Starr 2005).

Vaginal cleansing with povidone iodine solution reduces the risk of post-cesarean endometritis from 7.2% in control groups to 3.6% in vaginal cleansing groups (risk ratio (RR) 0.53, 95% confidence interval (CI) 0.35 to 0.79, five trials, 1766 women), fixed-effect meta-analysis. Because of high heterogeneity (I^2 = 65% and Tau^2 = 0.58), we used random-effects analysis to produce an overall summary for this outcome (average RR 0.39, 95% CI 0.16 to 0.97), *see* Analysis 1.1. The substantial heterogeneity indicates that treatment effects vary between studies, so we investigated the factors affecting treatment effects by the prespecified subgroup analyses (see below). As all of the trials did not include all subgroups, it is unclear if the subgroup analyses were able to account for all of the heterogeneity. However, we considered that the trials were similar enough clinically that the average treatment effect would be clinically meaningful. Vaginal cleansing did not lead to a statistically significant reduction in the outcomes of postoperative fever (RR 0.92, 95% CI 0.71 to 1.18, four trials, 1606 women, Analysis 1.2), wound infection (RR 0.99, 95% CI 0.57 to 1.70, four trials, 1336 women, Analysis 1.3), any wound complication (RR 0.63, 95% CI 0.37 to 1.07, two trials, 729 women, Analysis 1.4), or the composite of endometritis or wound complication (RR 0.55, 95% CI 0.26 to 1.15, one trial, 299 women, Analysis 1.5). Because of nearly significant heterogeneity (I^2 = 27%) for the outcome of postoperative fever and the issues noted above, we repeated the analysis with a random-effects model, still demonstrating no significant difference in the rates of postoperative fever with the intervention (RR 0.91, 95% CI 0.66 to 1.25).

Subgroup analysis - women in labor versus women not in labor

Two trials (Haas 2010; Reid 2001) stratified data for women in labor versus not in labor. Both trials reported on the outcomes of endometritis and any wound complication. There was not a statistically significant reduction in either of these outcomes for women in labor (endometritis RR 0.63, 95% CI 0.18 to 2.25, two trials, 311 women; any wound complication RR 0.77, 95% CI 0.36 to 1.61, two trials 314 women), *see* Analysis 2.1; Analysis 2.4. All confidence intervals for the other outcomes overlapped 1.0 for the single trial reporting the other outcomes for women in labor (postoperative fever: RR 0.22, 95% CI 0.03 to 1.83,

one trial, 95 women; wound infection: RR 0.67, 95% CI 0.17 to 2.63, one trial, 95 women; endometritis or wound complication: RR 0.40, 95% CI 0.14 to 1.18, one trial, 95 women), *see* Analysis 2.2; Analysis 2.3; Analysis 2.5. The subgroup analysis for women who were not in labor before the cesarean delivery failed to demonstrate any statistically significant differences in outcomes, although the rate of endometritis in this group was higher after a vaginal cleansing than in the control group (3.7% in the vaginal cleansing group versus 2.0% in the control group; RR 1.40, 95% CI 0.20 to 9.86, two trials, 414 women), *see* Analysis 2.1. This result was mainly driven by the Reid 2001 study finding. There was not a statistically significant effect of vaginal cleansing for the other outcomes (postoperative fever: RR 0.42, 95% CI 0.04 to 4.58, one trial, 201 women; wound infection: RR 0.67, 95% CI 0.19 to 2.43, one trial, 195 women; any wound complication: RR 0.54, 95% CI 0.25 to 1.16, two trials, 415 women; endometritis or wound complication: RR 0.85, 95% CI 0.29 to 2.56, one trial, 204 women), *see* Analysis 2.2; Analysis 2.3; Analysis 2.4; Analysis 2.5.

There was also no evidence of any difference between subgroups according to the test for subgroup differences performed: Test for subgroup differences: $Chi^2 = 0.45$, df = 1 (P = 0.50), $I^2 = 0\%$, Analysis 2.1; $Chi^2 = 0.16$, df = 1 (P = 0.69), $I^2 = 0\%$, Analysis 2.2; $Chi^2 = 0.00$, df = 1 (P = 0.99), $I^2 = 0\%$, Analysis 2.3; $Chi^2 = 0.41$, df = 1 (P = 0.52), $I^2 = 0\%$, Analysis 2.4; $Chi^2 = 0.92$, df = 1 (P = 0.34), $I^2 = 0\%$, Analysis 2.5.

Subgroup analysis - women with ruptured membranes versus women with intact membranes

Two trials (Guzman 2002; Haas 2010) stratified data for women with ruptured membranes versus women without ruptured membranes. Both trials reported on the outcomes of endometritis and postoperative fever. There was a statistically significant reduction in the rate of endometritis for women receiving vaginal preparation with povidone-iodine solution preoperatively with ruptured membranes (1.4% in the vaginal cleansing group versus 15.4% in the control group; RR 0.13, 95% CI 0.02 to 0.66, two trials, 148 women), *see* Analysis 3.1. There were no statistically significant differences between the vaginal preparation and control groups in the other outcomes for women with ruptured membranes (wound infection: RR 1.50, 95% CI 0.52 to 4.32, two trials, 148 women; postoperative fever: RR 0.31, 95% CI 0.04 to 2.64, one trial, 76 women; any wound complication: RR 0.53, 95%CI 0.15 to 1.89, 1 trials, 76 women; endometritis or wound complication: RR 0.46, 95%CI 0.13 to 1.61, one trial, 76 women), *see* Analysis 3.3; Analysis 3.2; Analysis 3.4; Analysis 3.5. For women with intact membranes, the rate of postoperative endometritis was not significantly reduced in the vaginal preparation group (0.6% in the vaginal cleansing group versus 3.4% in the control group; RR 0.26, 95% CI 0.04 to 1.51, two trials, 312 women), *see* Analysis 3.1. All of the reported outcomes for women without ruptured membranes were not statistically significantly different between the vaginal preparation and control groups (postoperative fever: RR 0.28, 95% CI 0.03 to 2.69, one trial, 224 women; wound infection: RR 0.67, 95% CI 0.23 to 1.89, two trials, 312 women; any wound complication: RR 0.73, 95% CI 0.25 to 2.10, one trial, 224 women; endometritis or wound complication: RR 0.66, 95% CI 0.26 to 1.72, one trial, 224 women), *see* Analysis 3.2; Analysis 3.3; Analysis 3.4; Analysis 3.5.

There was also no evidence of any difference between subgroups according to the test for subgroup differences performed: Test for subgroup differences: $Chi^2 = 0.33$, df = 1 (P = 0.57), $I^2 = 0\%$, Analysis 3.1; $Chi^2 = 0.00$, df = 1 (P = 0.96), $I^2 = 0\%$, Analysis 3.2; $Chi^2 = 1.15$, df = 1 (P = 0.28), $I^2 = 12.7\%$, Analysis 3.3; $Chi^2 = 0.14$, df = 1 (P = 0.70), $I^2 = 0\%$, Analysis 3.4; $Chi^2 = 0.20$, df = 1 (P = 0.66), $I^2 = 0\%$, Analysis 3.5.

Other subgroups - women with chorioamnionitis preoperatively versus women without chorioamnionitis; women undergoing emergency cesarean versus those undergoing unscheduled cesarean versus those undergoing scheduled cesarean; women with internal fetal or uterine monitors in place versus those with only external monitors in place before the cesarean

Neither of the two trials that included women diagnosed with chorioamnionitis stratified their data based on the presence or absence of chorioamnionitis. Neither of the two trials that did not exclude women undergoing emergency cesarean stratified their data based on emergency cesarean versus unscheduled versus scheduled cesarean. In addition, while two trials reported on the presence of internal monitoring (Haas 2010; Starr 2005), none of them stratified their outcome data based on this variable. Thus we did not perform these three subgroup analyses.

No adverse events were noted in any of the trials from the vaginal preparation solution.

DISCUSSION

Summary of main results

Vaginal cleansing with povidone-iodine solutions before cesarean delivery can reduce the incidence of post-cesarean endometritis. The heterogeneity in the results for this variable may be explainable by the study design and patient populations. The Guzman 2002 study used a placebo vaginal saline wash. This may have led to a lower baseline incidence of postoperative morbidity. The Haas 2010 study contained a majority of women who were obtaining planned repeat cesarean deliveries, a group known to be at lower risk for postoperative infectious morbidities. The subgroup analyses demonstrated that the reduction in postoperative endometritis

is most pronounced for women with ruptured membranes. This subgroup analysis should be interpreted with caution, however, as the number of participants and events is low. Thus, the intervention may be particularly useful for cesareans performed for women who have ruptured membranes. Ruptured membranes are a known risk factor for post-cesarean infectious morbidity. The use of vaginal preparation in women with ruptured membranes thus makes particular sense.

Overall completeness and applicability of evidence

The evidence is relatively complete, consistent, and highly applicable to clinical care.

Quality of the evidence

The risk of bias of the five included trials is reasonably low, with very few areas being identified as potential sources of bias (Figure 1; Figure 2). The agreement of the trial data in general and the large number of participants represented lend validity to the results of the meta-analysis. The clinical heterogeneity was essentially eliminated in the subgroup analyses, the results of which were consistent with the overall group results. Thus, fixed-effect modeling was retained in the overall results. The quality of the evidence using GRADE was low for post-cesarean endometritis due to high heterogeneity and a small sample size, moderate for postoperative fever due to the confidence interval crossing the line of no effect, and low for wound infection due to optimal information size that was not met (Summary of findings for the main comparison).

Potential biases in the review process

There is always potential that the review process was biased. However, the trial search yielded several studies. The study evaluation and data extraction were performed by three review authors with almost no discrepancies that needed to be resolved by consensus. Thus there is a minimal risk of bias in the review process. The studies were carried out in both developed and developing countries.

Agreements and disagreements with other studies or reviews

This review is limited by the somewhat small number of trials of preoperative vaginal preparation immediately before cesarean delivery. Because cesarean deliveries are so commonly performed and this intervention would seem to be an inexpensive, simple intervention to reduce post-cesarean infectious morbidities, it was surprising to find such a paucity of randomized trial data. While the data point to a reduction in post-cesarean endometritis with the intervention, it is possible that with more trial data, the trends towards other reduced infectious morbidity would also become statistically significant. Uniformity in the reporting of the data outcomes and the subgroup data stratification would have also aided this review.

AUTHORS' CONCLUSIONS

Implications for practice

Vaginal preparation with povidone-iodine solution immediately before cesarean delivery reduces the risk of postoperative endometritis. No adverse effects were noted in any of the trials. This benefit is particularly realized for women undergoing cesarean delivery with ruptured membranes. As a simple, generally inexpensive intervention, providers should consider implementing preoperative vaginal cleansing with povidone-iodine before performing cesarean deliveries. Information on whether other methods of, or solutions for, vaginal preparation is lacking.

Implications for research

As practice changes and providers begin to routinely implement preoperative vaginal cleansing before cesarean deliveries, postoperative infectious morbidities should be tracked and compared with the same outcomes before the practice change. Any adverse events realized with implementation should be reported.

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As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Asghania 2011

Methods	Double blind quasi-RCT.
Participants	Women undergoing non-emergent or laboring cesarean delivery.
Interventions	Two 4x4 gauze sponges soaked in 10% povidone iodine solutions rotated 360 degrees for 30 seconds from vault to introitus vs. no vaginal scrub
Outcomes	Febrile morbidity, endometritis, wound infection.
Notes	May 2007-April 2008.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quasi-randomized, alternating sequence.
Allocation concealment (selection bias)	High risk	Quasi-randomized, alternating sequence.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants: unclear.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Complete outcome data.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Other bias	High risk	Large differences in baseline characteristics- more examinations, longer labor, more preterm, longer surgery, longer duration of PROM in vaginal cleansing group

Guzman 2002

Methods	RCT.
Participants	160 women undergoing cesarean delivery (80 intervention, 80 control)
Interventions	Intervention: povidone-iodine vaginal wash (concentration not specified) Control: saline vaginal wash.
Outcomes	Endometritis (temperature > 100.4 degrees F at least twice > 24 hours after surgery or of 101 degrees F any time after surgery, with abdominal/uterine tenderness) Cellulitis (advancing erythema around the incision).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not specified.
Allocation concealment (selection bias)	Unclear risk	Not specified.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Cleansing done by nurse while providers outside and thus providers were blinded to the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessors blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete outcome data.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Other bias	Low risk	No evidence of other bias.

Haas 2010

Methods	RCT.
Participants	300 participants (155 intervention, 145 control) received vaginal cleansing or nothing directly before cesarean delivery, age $\geq$ 18 years
Interventions	Intervention: preoperative vaginal cleansing with 1% povidone iodine scrubs Control: no preoperative vaginal cleansing.

Haas 2010 (*Continued*)

Outcomes	Post-cesarean endometritis (uterine tenderness plus postoperative fever requiring antibiotics) Postoperative fever (> 38 degrees Celcius, > 24 hours after surgery) Wound infection requiring antibiotics. Wound separation, seroma, hematoma, or need for debridement. Composite infectious morbidity outcome: either endometritis, fever, sepsis, hospital readmission, wound infection, or wound complication
Notes	Internally funded. The trial was stopped early due to difficulty recruiting.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number table, replacement randomization
Allocation concealment (selection bias)	Low risk	Sequentially numbered opaque security envelopes.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Not specifically blinded but after anesthesia care providers did not necessarily know group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessor only.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Appeared to be complete data on all participants.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Other bias	Unclear risk	Trial stopped early at safety analysis due to difficulty recruiting and effect seen

Reid 2001

Methods	RCT.
Participants	501 women admitted and mentally competent to consent for a cesarean delivery (250 intervention, 251 control)
Interventions	Intervention: 10% povidone-iodine surgical scrub solution vaginally immediately before cesarean Control: no preparation.

Outcomes	Fever (38C or greater after the day of surgery). Febrile morbidity (postoperative fever on 2 or more calendar days, excluding the day of surgery) Endometritis (postoperative fever, with a physician's note indicating uterine or abdominal pain or tenderness, preceding an order for antibiotics and a statement indicating that the antibiotics were for uterine or pelvic infection and laboratory studies did not indicate other source for the infection) Wound separation (defined by chart note reporting separation of the operative incision requiring intervention) Number of postoperative days with fever. Average duration of antibiotic administration. Length of hospitalization.
Notes	Chorioamnionitis participants excluded from analysis.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated, permuted block randomization schedule.
Allocation concealment (selection bias)	Low risk	Opaque sealed and numbered envelopes taped to abdominal prep packs
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not specifically stated. Cleansing done by residents during routine prep. These may have been the same surgeons who did the surgery and postoperative care
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessor masked.
Incomplete outcome data (attrition bias) All outcomes	High risk	Excluded 68 women post-hoc with antenatal chorioamnionitis because inclusion distorted the absolute rates of fever and infectious complications
Selective reporting (reporting bias)	High risk	One trial (Reid 2001) had a large number of participants excluded after randomization who had chorioamnionitis (a known risk factor for postoperative infectious morbidity) because their inclusion "distorted the absolute rates of fever and infectious morbidity." That trial states that when the 68 participants with antepartum infection were included, the estimates of effect of vaginal preparation were not meaningfully different. Thus they planned to exclude those participants from reports of outcomes. As this represented 13.5% of the originally randomized sample, however, there is a risk that this introduced selective reporting bias into the trial (Reid 2001).

Other bias	Low risk	No evidence of other bias.

Starr 2005

Methods	RCT.
Participants	400 women to undergo non-emergency cesarean delivery (142 intervention, 166 control analyzed)
Interventions	Intervention: pre-packaged povidone-iodine solution (EZ Prep 200, 5%) vaginal preparation for 30 seconds Control: no preoperative vaginal preparation.
Outcomes	Febrile morbidity (any postoperative temperature > 38C). Endometritis (temperature elevation > 38C beyond the first postoperative day, in association with uterine tenderness and foul lochia, in the absence of evidence of other infection; given at the time of clinical evaluation) Wound infection (clinical diagnosis evidenced by erythema or wound edge separation with purulent drainage; including wound dehiscence and necrotizing fasciitis and excluding skin separation without evidence of cellulitis)
Notes	Excluded chorioamnionitis and placenta previa.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random digit table.
Allocation concealment (selection bias)	Low risk	Sequentially numbered, opaque, sealed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Not stated for participants but treating providers at the time of fever were unaware of participation status
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Chart reviewer unaware of group.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Ultimately 92 participants excluded from analysis, reasons explained. Unclear if exclusions impacted data
Selective reporting (reporting bias)	Unclear risk	One other trial had a potential selective reporting bias (Starr 2005). Of 400 participants randomized, 92 (23%) were excluded after randomization: 33 due to lost envelopes, 6 for violations of inclusion criteria, and 53 because their hospital charts could not be located. Of all the women excluded, 54 were in the

		vaginal cleansing group and 38 were in the control group. Only outcomes for women for whom all data were available were reported. The large number of women excluded also makes this trial subject to an unclear risk of bias, however as there is no outcome data for the excluded participants, the potential impact is unclear (Starr 2005).
Other bias	Low risk	No evidence of other bias.

PROM: premature rupture of membranes
RCT: randomized controlled trial
vs: versus

DATA AND ANALYSES

Comparison 1. Vaginal preparation versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Post-cesarean endometritis	5	1766	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.16, 0.97]
2 Postoperative fever	4	1606	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.71, 1.18]
3 Wound infection	4	1336	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.57, 1.70]
4 Any wound complication	2	729	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.37, 1.07]
5 Composite wound complication or endometritis	1	299	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.26, 1.15]

Comparison 2. Vaginal preparation versus control - stratified by presence of labor

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Post-cesarean endometritis	2	725	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.36, 2.44]
1.1 Women in labor	2	311	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.18, 2.25]
1.2 Women not in labor	2	414	Risk Ratio (M-H, Random, 95% CI)	1.40 [0.20, 9.86]
2 Postoperative fever	1	296	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.06, 1.37]
2.1 Women in labor	1	95	Risk Ratio (M-H, Fixed, 95% CI)	0.22 [0.03, 1.83]
2.2 Women not in labor	1	201	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.04, 4.58]
3 Wound infection	1	290	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.26, 1.71]
3.1 Women in labor	1	95	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.17, 2.63]
3.2 Women not in labor	1	195	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.19, 2.43]
4 Any wound complication	2	729	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.38, 1.09]
4.1 Women in labor	2	314	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.36, 1.61]
4.2 Women not in labor	2	415	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.25, 1.16]
5 Composite wound complication or endometritis	1	299	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.27, 1.23]
5.1 Women in labor	1	95	Risk Ratio (M-H, Fixed, 95% CI)	0.40 [0.14, 1.18]
5.2 Women not in labor	1	204	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.29, 2.56]

Comparison 3. Vaginal preparation versus control - stratified by presence of ruptured membranes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Post-cesarean endometritis	2	460	Risk Ratio (M-H, Fixed, 95% CI)	0.17 [0.05, 0.56]
1.1 Women with ruptured membranes	2	148	Risk Ratio (M-H, Fixed, 95% CI)	0.13 [0.02, 0.66]
1.2 Women with intact membranes	2	312	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.04, 1.51]
2 Postoperative fever	1	300	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.06, 1.40]
2.1 Women with ruptured membranes	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.04, 2.64]
2.2 Women with intact membranes	1	224	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.03, 2.69]
3 Wound infection	2	460	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.48, 2.06]
3.1 Women with ruptured membranes	2	148	Risk Ratio (M-H, Fixed, 95% CI)	1.5 [0.52, 4.32]
3.2 Women with intact membranes	2	312	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.23, 1.89]
4 Any wound complication	1	300	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.28, 1.44]
4.1 Women with ruptured membranes	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.15, 1.89]
4.2 Women with intact membranes	1	224	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.25, 2.10]
5 Composite wound complication or endometritis	1	300	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.27, 1.23]
5.1 Women with ruptured membranes	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.13, 1.61]
5.2 Women with intact membranes	1	224	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.26, 1.72]

Analysis 1.1. Comparison 1 Vaginal preparation versus control, Outcome 1 Post-cesarean endometritis.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 1 Vaginal preparation versus control

Outcome: 1 Post-cesarean endometritis

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Asghania 2011	1/284	7/284		12.4 %	0.14 [0.02, 1.15]
Guzman 2002	2/80	13/80		18.8 %	0.15 [0.04, 0.66]
Haas 2010	0/155	4/145		7.7 %	0.10 [0.01, 1.91]
Reid 2001	19/217	16/213		31.0 %	1.17 [0.62, 2.21]
Starr 2005	10/142	24/166		30.0 %	0.49 [0.24, 0.98]
Total (95% CI)	**878**	**888**		**100.0 %**	**0.39 [0.16, 0.97]**

Total events: 32 (Vaginal preparation), 64 (Control)

Heterogeneity: $Tau^2 = 0.58$; $Chi^2 = 11.45$, df = 4 (P = 0.02); $I^2 = 65\%$

Test for overall effect: Z = 2.03 (P = 0.043)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Vaginal preparation versus control, Outcome 2 Postoperative fever.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 1 Vaginal preparation versus control

Outcome: 2 Postoperative fever

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Asghania 2011	14/284	17/284		16.2 %	0.82 [0.41, 1.64]
Haas 2010	2/155	7/145		6.9 %	0.27 [0.06, 1.27]
Reid 2001	44/217	37/213		35.6 %	1.17 [0.79, 1.73]
Starr 2005	34/142	47/166		41.3 %	0.85 [0.58, 1.24]
Total (95% CI)	**798**	**808**		**100.0 %**	**0.92 [0.71, 1.18]**

Total events: 94 (Vaginal preparation), 108 (Control)

Heterogeneity: $Chi^2 = 4.12$, df = 3 (P = 0.25); $I^2 = 27\%$

Test for overall effect: Z = 0.68 (P = 0.49)

Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Vaginal preparation versus control, Outcome 3 Wound infection.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 1 Vaginal preparation versus control

Outcome: 3 Wound infection

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Asghania 2011	10/284	9/284		35.7 %	1.11 [0.46, 2.69]
Guzman 2002	7/80	4/80		15.9 %	1.75 [0.53, 5.75]
Haas 2010	7/155	10/145		41.0 %	0.65 [0.26, 1.67]
Starr 2005	1/142	2/166		7.3 %	0.58 [0.05, 6.38]
Total (95% CI)	**661**	**675**		**100.0 %**	**0.99 [0.57, 1.70]**

Total events: 25 (Vaginal preparation), 25 (Control)

Heterogeneity: Chi^2 = 1.88, df = 3 (P = 0.60); I^2 =0.0%

Test for overall effect: Z = 0.05 (P = 0.96)

Test for subgroup differences: Not applicable

Analysis 1.4. Comparison 1 Vaginal preparation versus control, Outcome 4 Any wound complication.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 1 Vaginal preparation versus control

Outcome: 4 Any wound complication

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Haas 2010	9/155	14/144		44.4 %	0.60 [0.27, 1.34]
Reid 2001	12/217	18/213		55.6 %	0.65 [0.32, 1.33]
Total (95% CI)	**372**	**357**		**100.0 %**	**0.63 [0.37, 1.07]**

Total events: 21 (Vaginal preparation), 32 (Control)

Heterogeneity: Chi^2 = 0.03, df = 1 (P = 0.87); I^2 =0.0%

Test for overall effect: Z = 1.71 (P = 0.087)

Test for subgroup differences: Not applicable

Analysis 1.5. Comparison 1 Vaginal preparation versus control, Outcome 5 Composite wound complication or endometritis.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 1 Vaginal preparation versus control

Outcome: 5 Composite wound complication or endometritis

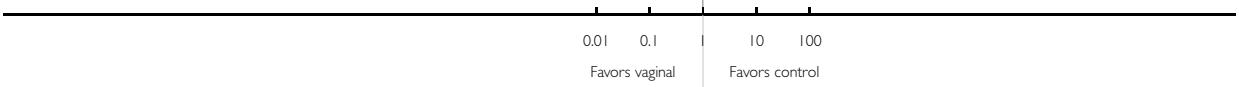
Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Haas 2010	10/155	17/144		100.0 %	0.55 [0.26, 1.15]
Total (95% CI)	**155**	**144**		**100.0 %**	**0.55 [0.26, 1.15]**

Total events: 10 (Vaginal preparation), 17 (Control)

Heterogeneity: not applicable

Test for overall effect: Z = 1.58 (P = 0.11)

Test for subgroup differences: Not applicable

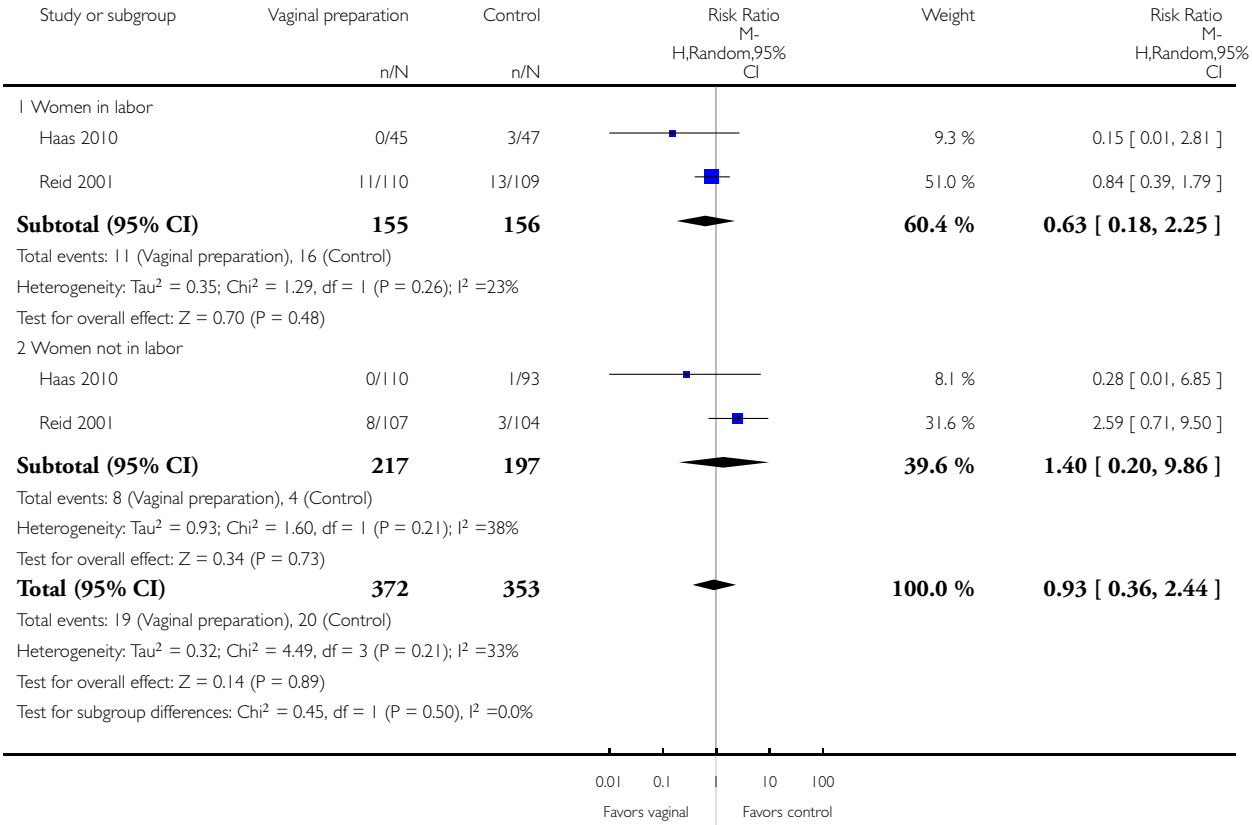


Analysis 2.1. Comparison 2 Vaginal preparation versus control - stratified by presence of labor, Outcome 1 Post-cesarean endometritis.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 2 Vaginal preparation versus control - stratified by presence of labor

Outcome: 1 Post-cesarean endometritis



Analysis 2.2. Comparison 2 Vaginal preparation versus control - stratified by presence of labor, Outcome 2 Postoperative fever.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 2 Vaginal preparation versus control - stratified by presence of labor

Outcome: 2 Postoperative fever

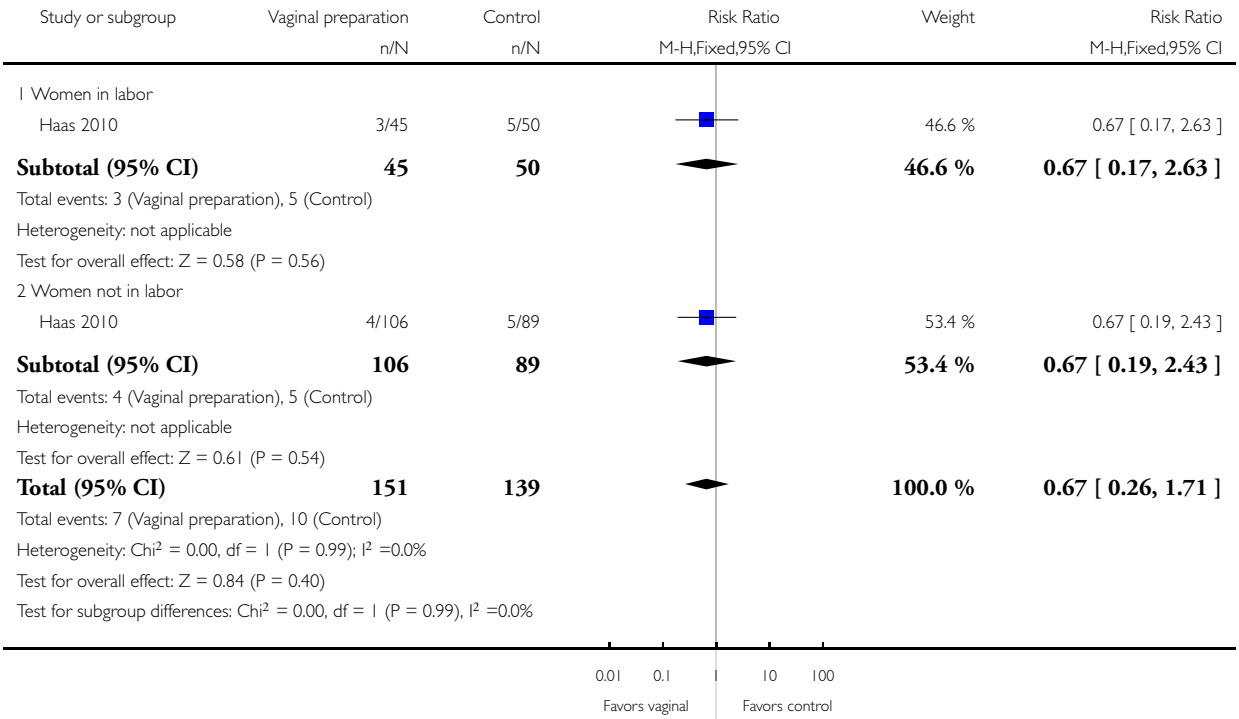
Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Women in labor					
Haas 2010	1/45	5/50		68.6 %	0.22 [0.03, 1.83]
Subtotal (95% CI)	**45**	**50**		**68.6 %**	**0.22 [0.03, 1.83]**
Total events: 1 (Vaginal preparation), 5 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.40 (P = 0.16)					
2 Women not in labor					
Haas 2010	1/109	2/92		31.4 %	0.42 [0.04, 4.58]
Subtotal (95% CI)	**109**	**92**		**31.4 %**	**0.42 [0.04, 4.58]**
Total events: 1 (Vaginal preparation), 2 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.71 (P = 0.48)					
Total (95% CI)	**154**	**142**		**100.0 %**	**0.28 [0.06, 1.37]**
Total events: 2 (Vaginal preparation), 7 (Control)					
Heterogeneity: Chi^2 = 0.16, df = 1 (P = 0.69); I^2 =0.0%					
Test for overall effect: Z = 1.57 (P = 0.12)					
Test for subgroup differences: Chi^2 = 0.16, df = 1 (P = 0.69), I^2 =0.0%					

Analysis 2.3. Comparison 2 Vaginal preparation versus control - stratified by presence of labor, Outcome 3 Wound infection.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 2 Vaginal preparation versus control - stratified by presence of labor

Outcome: 3 Wound infection



Analysis 2.4. Comparison 2 Vaginal preparation versus control - stratified by presence of labor, Outcome 4 Any wound complication.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 2 Vaginal preparation versus control - stratified by presence of labor

Outcome: 4 Any wound complication

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Women in labor					
Haas 2010	4/45	8/50		23.5 %	0.56 [0.18, 1.72]
Reid 2001	7/110	7/109		21.8 %	0.99 [0.36, 2.73]
Subtotal (95% CI)	**155**	**159**		**45.3 %**	**0.77 [0.36, 1.61]**
Total events: 11 (Vaginal preparation), 15 (Control)					
Heterogeneity: Chi^2 = 0.56, df = 1 (P = 0.46); I^2 =0.0%					
Test for overall effect: Z = 0.70 (P = 0.48)					
2 Women not in labor					
Haas 2010	5/110	6/94		20.1 %	0.71 [0.22, 2.26]
Reid 2001	5/107	11/104		34.6 %	0.44 [0.16, 1.23]
Subtotal (95% CI)	**217**	**198**		**54.7 %**	**0.54 [0.25, 1.16]**
Total events: 10 (Vaginal preparation), 17 (Control)					
Heterogeneity: Chi^2 = 0.37, df = 1 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 1.58 (P = 0.11)					
Total (95% CI)	**372**	**357**		**100.0 %**	**0.64 [0.38, 1.09]**
Total events: 21 (Vaginal preparation), 32 (Control)					
Heterogeneity: Chi^2 = 1.31, df = 3 (P = 0.73); I^2 =0.0%					
Test for overall effect: Z = 1.63 (P = 0.10)					
Test for subgroup differences: Chi^2 = 0.41, df = 1 (P = 0.52), I^2 =0.0%					

Analysis 2.5. Comparison 2 Vaginal preparation versus control - stratified by presence of labor, Outcome 5 Composite wound complication or endometritis.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 2 Vaginal preparation versus control - stratified by presence of labor

Outcome: 5 Composite wound complication or endometritis

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Women in labor					
Haas 2010	4/45	11/50		61.7 %	0.40 [0.14, 1.18]
Subtotal (95% CI)	**45**	**50**		**61.7 %**	**0.40 [0.14, 1.18]**
Total events: 4 (Vaginal preparation), 11 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.66 (P = 0.097)					
2 Women not in labor					
Haas 2010	6/110	6/94		38.3 %	0.85 [0.29, 2.56]
Subtotal (95% CI)	**110**	**94**		**38.3 %**	**0.85 [0.29, 2.56]**
Total events: 6 (Vaginal preparation), 6 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.28 (P = 0.78)					
Total (95% CI)	**155**	**144**		**100.0 %**	**0.58 [0.27, 1.23]**
Total events: 10 (Vaginal preparation), 17 (Control)					
Heterogeneity: Chi^2 = 0.92, df = 1 (P = 0.34); I^2 =0.0%					
Test for overall effect: Z = 1.43 (P = 0.15)					
Test for subgroup differences: Chi^2 = 0.92, df = 1 (P = 0.34), I^2 =0.0%					

Analysis 3.1. Comparison 3 Vaginal preparation versus control - stratified by presence of ruptured membranes, Outcome 1 Post-cesarean endometritis.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 3 Vaginal preparation versus control - stratified by presence of ruptured membranes

Outcome: 1 Post-cesarean endometritis

Study or subgroup	Vaginal cleansing n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Women with ruptured membranes					
Guzman 2002	1/36	10/36		55.7 %	0.10 [0.01, 0.74]
Haas 2010	0/34	2/42		12.5 %	0.25 [0.01, 4.95]
Subtotal (95% CI)	**70**	**78**		**68.2 %**	**0.13 [0.02, 0.66]**
Total events: 1 (Vaginal cleansing), 12 (Control)					
Heterogeneity: Chi^2 = 0.24, df = 1 (P = 0.62); I^2 =0.0%					
Test for overall effect: Z = 2.46 (P = 0.014)					
2 Women with intact membranes					
Guzman 2002	1/44	3/44		16.7 %	0.33 [0.04, 3.08]
Haas 2010	0/121	2/103		15.0 %	0.17 [0.01, 3.51]
Subtotal (95% CI)	**165**	**147**		**31.8 %**	**0.26 [0.04, 1.51]**
Total events: 1 (Vaginal cleansing), 5 (Control)					
Heterogeneity: Chi^2 = 0.12, df = 1 (P = 0.73); I^2 =0.0%					
Test for overall effect: Z = 1.50 (P = 0.13)					
Total (95% CI)	**235**	**225**		**100.0 %**	**0.17 [0.05, 0.56]**
Total events: 2 (Vaginal cleansing), 17 (Control)					
Heterogeneity: Chi^2 = 0.68, df = 3 (P = 0.88); I^2 =0.0%					
Test for overall effect: Z = 2.92 (P = 0.0035)					
Test for subgroup differences: Chi^2 = 0.33, df = 1 (P = 0.57), I^2 =0.0%					

Analysis 3.2. Comparison 3 Vaginal preparation versus control - stratified by presence of ruptured membranes, Outcome 2 Postoperative fever.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 3 Vaginal preparation versus control - stratified by presence of ruptured membranes

Outcome: 2 Postoperative fever

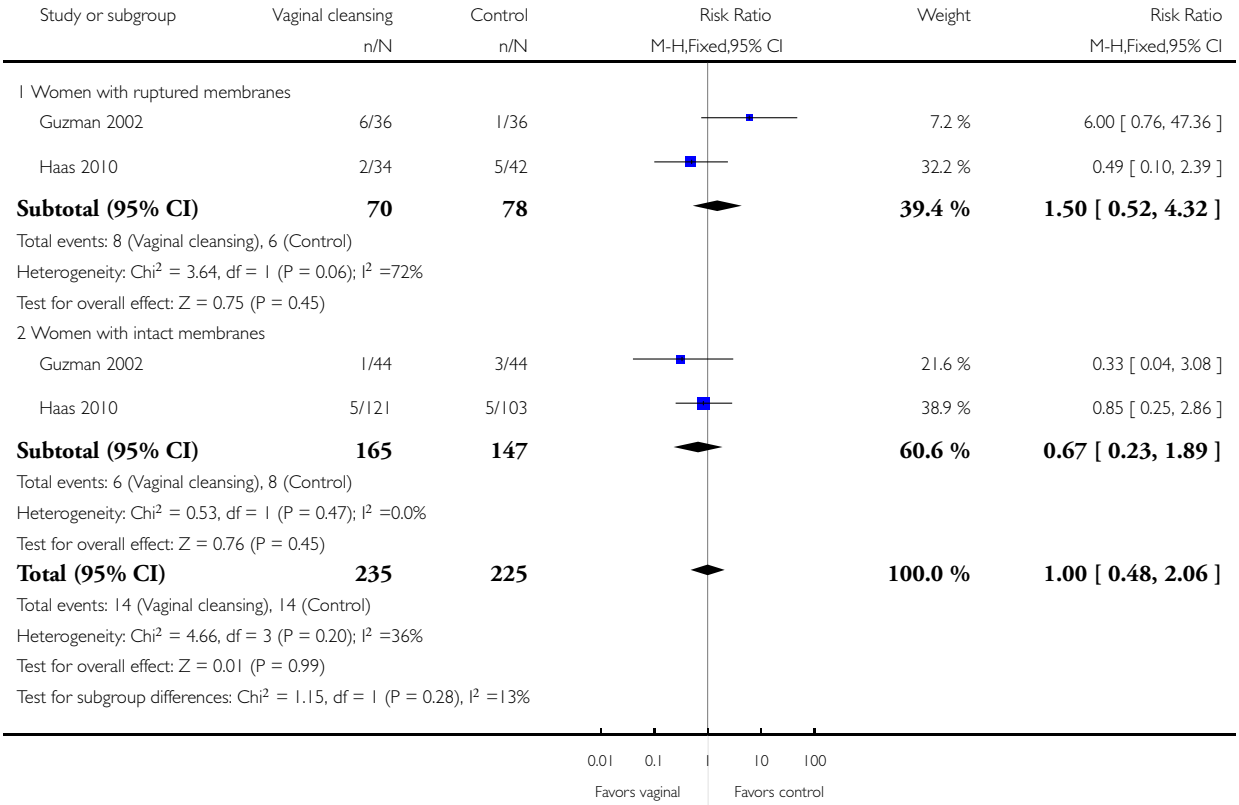
Study or subgroup	Vaginal cleansing n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Women with ruptured membranes					
Haas 2010	1/34	4/42		52.5 %	0.31 [0.04, 2.64]
Subtotal (95% CI)	**34**	**42**		**52.5 %**	**0.31 [0.04, 2.64]**
Total events: 1 (Vaginal cleansing), 4 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.07 (P = 0.28)					
2 Women with intact membranes					
Haas 2010	1/121	3/103		47.5 %	0.28 [0.03, 2.69]
Subtotal (95% CI)	**121**	**103**		**47.5 %**	**0.28 [0.03, 2.69]**
Total events: 1 (Vaginal cleansing), 3 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.10 (P = 0.27)					
Total (95% CI)	**155**	**145**		**100.0 %**	**0.30 [0.06, 1.40]**
Total events: 2 (Vaginal cleansing), 7 (Control)					
Heterogeneity: Chi^2 = 0.00, df = 1 (P = 0.96); I^2 =0.0%					
Test for overall effect: Z = 1.53 (P = 0.13)					
Test for subgroup differences: Chi^2 = 0.00, df = 1 (P = 0.96), I^2 =0.0%					

Analysis 3.3. Comparison 3 Vaginal preparation versus control - stratified by presence of ruptured membranes, Outcome 3 Wound infection.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 3 Vaginal preparation versus control - stratified by presence of ruptured membranes

Outcome: 3 Wound infection

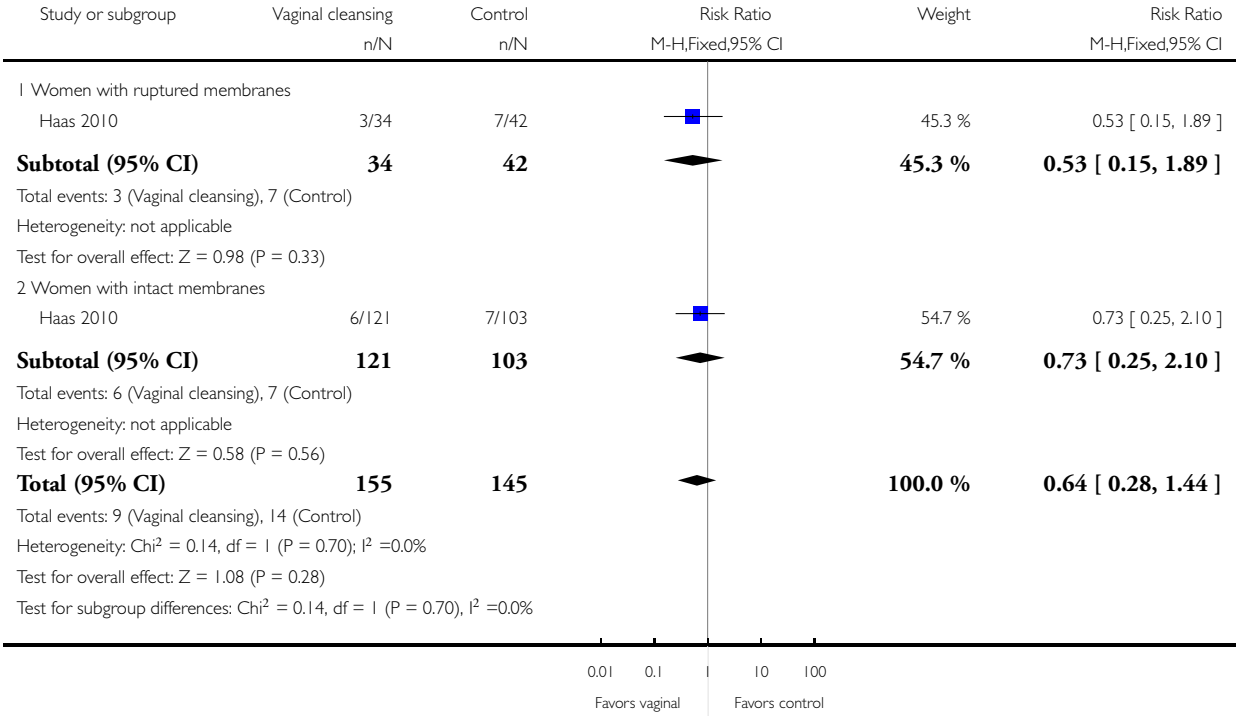


Analysis 3.4. Comparison 3 Vaginal preparation versus control - stratified by presence of ruptured membranes, Outcome 4 Any wound complication.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 3 Vaginal preparation versus control - stratified by presence of ruptured membranes

Outcome: 4 Any wound complication



Analysis 3.5. Comparison 3 Vaginal preparation versus control - stratified by presence of ruptured membranes, Outcome 5 Composite wound complication or endometritis.

Review: Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

Comparison: 3 Vaginal preparation versus control - stratified by presence of ruptured membranes

Outcome: 5 Composite wound complication or endometritis

Study or subgroup	Vaginal cleansing n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Women with ruptured membranes					
Haas 2010	3/34	8/42		42.4 %	0.46 [0.13, 1.61]
Subtotal (95% CI)	**34**	**42**		**42.4 %**	**0.46 [0.13, 1.61]**
Total events: 3 (Vaginal cleansing), 8 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.21 (P = 0.23)					
2 Women with intact membranes					
Haas 2010	7/121	9/103		57.6 %	0.66 [0.26, 1.72]
Subtotal (95% CI)	**121**	**103**		**57.6 %**	**0.66 [0.26, 1.72]**
Total events: 7 (Vaginal cleansing), 9 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.85 (P = 0.40)					
Total (95% CI)	**155**	**145**		**100.0 %**	**0.58 [0.27, 1.23]**
Total events: 10 (Vaginal cleansing), 17 (Control)					
Heterogeneity: Chi^2 = 0.20, df = 1 (P = 0.66); I^2 =0.0%					
Test for overall effect: Z = 1.43 (P = 0.15)					
Test for subgroup differences: Chi^2 = 0.20, df = 1 (P = 0.66), I^2 =0.0%					

APPENDICES

Appendix 1. Methods used to be used in future updates

Data collection and analysis

Selection of studies

At least two review authors will independently assess for inclusion all the potential studies we identify as a result of the search strategy. We will resolve any disagreement through discussion or, if required, we will consult a third author.
We will create a study flow diagram to map out the number of records identified, included and excluded.

Data extraction and management

We will design a form to extract data. For eligible studies, at least two review authors will extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult a third author. We will enter data into Review Manager software (RevMan 2014) and check for accuracy.
When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will resolve any disagreement by discussion or by involving a third assessor.

(1) Random sequence generation (checking for possible selection bias)

We will describe for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.
We will assess the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We will describe for each included study the method used to conceal allocation to interventions prior to assignment and will assess whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.
We will assess the methods as:

- low risk of bias (e.g. telephone or central randomization; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We will describe for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We will consider that studies are at low risk of bias if they were blinded, or if we judge that the lack of blinding would be unlikely to affect results. We will assess blinding separately for different outcomes or classes of outcomes.
We will assess the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We will describe for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We will assess blinding separately for different outcomes or classes of outcomes.
We will assess methods used to blind outcome assessment as:

- low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomized participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses which we undertake.
We will assess methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomization);
- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We will describe for each included study how we investigated the possibility of selective outcome reporting bias and what we found. We will assess the methods as:

- low risk of bias (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We will describe for each included study any important concerns we have about other possible sources of bias.
We will assess whether each study was free of other problems that could put it at risk of bias:

- low risk of other bias;
- high risk of other bias;
- unclear whether there is risk of other bias.

(7) Overall risk of bias

We will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

Measures of treatment effect

Dichotomous data

For dichotomous data, we will present results as summary risk ratio with 95% confidence intervals.

Continuous data

For continuous data, we will use the mean difference if outcomes are measured in the same way between trials. We will use the standardized mean difference to combine trials that measure the same outcome, but use different methods.

Unit of analysis issues

Cluster-randomized trials

We will include cluster-randomized trials in the analyses along with individually-randomized trials. We will adjust their sample sizes using the methods described in the *Handbook* [Section 16.3.4 or 16.3.6] using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomized trials and individually-randomized trials, we plan to synthesize the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomization unit is considered to be unlikely.
We will also acknowledge heterogeneity in the randomization unit and perform a sensitivity analysis to investigate the effects of the randomization unit.

Cross-over trials

We determined that it was not possible to include cross-over trials in this review.

Other unit of analysis issues

Dealing with missing data

For included studies, we will note levels of attrition. We will explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.
For all outcomes, we will carry out analyses, as far as possible, on an intention-to-treat basis, i.e. we will attempt to include all participants randomized to each group in the analyses, and all participants will be analyzed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial will be the number randomized minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

We will assess statistical heterogeneity in each meta-analysis using the Tau^2, I^2 and Chi^2 statistics. We will regard heterogeneity as substantial if an I^2 is greater than 30% and either a Tau^2 is greater than zero, or there is a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

If there are 10 or more studies in the meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually. If asymmetry is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We will carry out statistical analysis using the Review Manager software (RevMan 2014). We will use fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect: i.e. where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials is considered clinically meaningful. The random-effects summary will be treated as the average of the range of possible treatment effects and we will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful, we will not combine trials.

If we use random-effects analyses, the results will be presented as the average treatment effect with 95% confidence intervals, and the estimates of Tau^2 and I^2.

Subgroup analysis and investigation of heterogeneity

We plan to carry out the following subgroup analyses for primary outcomes:

1. cesarean after labor versus cesarean with no preceding labor;
2. ruptured membranes versus intact membranes;
3. chorioamnionitis versus no chorioamnionitis;
4. emergency versus unscheduled versus scheduled cesarean delivery;
5. intrapartum internal monitoring devices versus no internal monitoring devices.

We will assess subgroup differences by interaction tests available within RevMan (RevMan 2014). We will report the results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2 value.

Sensitivity analysis

We plan to perform sensitivity analyses to explore the effect of study quality relating to the 'Risk of bias' items including allocation concealment, incomplete data collection to assess for any substantive difference to the overall result. If cluster-randomized trials are included in the review, we aim to apply other sensitivity analysis incorporating an estimate of the ICC taken from a different study, to see what the effect of different values of the ICC on the results of the analysis would be.

WHAT'S NEW

Last assessed as up-to-date: 21 July 2014.

Date	Event	Description
21 July 2014	New search has been performed	Search updated. No new trial reports identified.
21 July 2014	New citation required but conclusions have not changed	Review updated.

HISTORY

Protocol first published: Issue 3, 2009

Review first published: Issue 3, 2010

Date	Event	Description
14 September 2012	New citation required but conclusions have not changed	Review updated.
14 September 2012	New search has been performed	Search updated. One new trial included (Asghania 2011) and the published report of Haas 2010 added.

CONTRIBUTIONS OF AUTHORS

All review authors helped develop the protocol, data extraction, and preparation of results and final report.

DECLARATIONS OF INTEREST

There are no financial conflicts of interest to disclose. David Haas is the Principal Investigator for a randomized trial included in this review (Haas 2010). Sarah Morgan is also an investigator in the same trial. Trial authors were not involved in assessing trial quality or extracting data from the Haas 2010 study, this was carried out by the third review author, Karenrose Contreras and a third party (Dr Jon Hathaway, MD, PhD).

SOURCES OF SUPPORT

Internal sources

- Indiana University School of Medicine, Indianapolis, USA.

External sources

- UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research (RHR), World Health Organization, Switzerland.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Three of the planned subgroup analyses were unable to be performed as they were not reported in the trials.

INDEX TERMS

Medical Subject Headings (MeSH)

Administration, Intravaginal; Anti-Infective Agents, Local [*administration & dosage]; Cesarean Section [*adverse effects]; Disinfection [*methods]; Endometritis [*prevention & control]; Povidone-Iodine [*administration & dosage]; Randomized Controlled Trials as Topic; Surgical Wound Infection [*prevention & control]; Vagina

MeSH check words

Female; Humans; Pregnancy